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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/351,778	07/12/1999	WILLIAM S. M. WOLD	16153-7775	1203

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EXAMINER	
PRIEBE, SCOTT DAVID	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 07/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/351,778	WOLD ET AL.	
	Examiner	Art Unit	
	Scott Priebe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-32* is/are pending in the application.

4a) Of the above claim(s) *6-9,16-19,23 and 25-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,10-13,20-22 and 32* is/are rejected.

7)☒ Claim(s) *5,14,15 and 24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *21,23* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply* .

DETAILED ACTION

The Group and/or Art Unit designation of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Primary Examiner Scott D. Priebe, Ph.D., Group Art Unit 1632.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/10/02 has been entered.

The amendments filed 1/10/02 and 4/17/02 have been entered. Claim 3 has been cancelled, claims 1-2, 4-5, 10-13, 15, and 24 have been amended, and claim 28 has been added as per the paper filed 1/10/02. Claims 29-32 have been added. as per the paper filed 4/17/02.

Election/Restriction

Claims 6-9, 16-19, 23 and 25-27 remain withdrawn and new claims 28-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made without

traverse in Paper No. 9. New claims 28-31 are directed to non-elected invention II, replication restricted adenoviral vectors.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Figure 18A contains an amino acid sequence, and Fig. 21 (sheets 1-11) contains a nucleotide sequence. However, the 'Brief Description' of these figures do not provide the SEQ ID NO assigned to these sequences. If the amino acid sequence of Fig. 18A is that of SEQ ID NO: 5, the description of Fig. 18A should indicate the SEQ ID NO. It does not appear that the Ad5 genome sequence presented in Fig. 21 has been included in the Sequence Listing, as required under 37 CFR 1.821 through 1.825. This sequence should be added to the Sequence Listing, and a substitute Sequence Listing provided.

Applicants are required to comply with all of the requirements of 37 CFR 1.821 through 37 CFR 1.825. *Any* response to this Office Action which fails to meet *all* of these requirements will be considered non-responsive. The nature of the sequence disclosed in the instant application has allowed an examination on the merits, the results of which are communicated below.

Claim Rejections - 35 USC § 102 & 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 2, 4, 10-12 and 32 re rejected under 35 U.S.C. 102(b) as being anticipated by Tollefson et al. (J. Virol., 70(4):2296-2306, 4/96), as evidenced by Bett et al. (Virus Res. 39: 75-82, 1995).

Tollefson et al. discloses an Ad5 replication-competent adenovirus capable of overexpressing an adenovirus death protein, expressing the E3 12.5K protein, and lacking expression of E3 proteins, including RIDα (also known as 10.4K), RIDβ (also known as 14.5K) and 14.7K (i.e. Ad5 dl309) and further disclose a method for promoting death of neoplastic cells in culture comprising infection of human A549 cells with said recombinant adenovirus (see e.g. Fig. 2 and "Materials and Methods"). Inasmuch as the dl309 is from an Ad5 strain, the disclosure of Tollefson anticipates the broadly claimed "variant" subject matter recited in claims 2 and 11, particularly as directed to SEQ ID NO:7 (or variants thereof).

The specification (page 12, lines 32-35) teaches that deletion of splicing signals for E3 transcripts will cause the adp protein to be "overexpressed". Ad5 *dl309* lacks splice sites for the transcripts for the 14.7K protein. See Bett et al., Fig. 1. The amendment to claim 1 no longer requires that replication be restricted to neoplastic cells. Replication-competent in neoplastic cells does not preclude replication competent in non-neoplastic cells.

Claims 1, 2, 4 and 10-13 remain rejected under 35 U.S.C. 102(e) as being clearly anticipated by Henderson et al. (U.S. 6,197,293, filed 3/02/98) for the reasons of record set forth in the Office action of 3/15/01.

Claims 1, 2, 4 and 10-13 remain rejected under 35 U.S.C. 102(e) as being clearly anticipated by Little et al. (U.S. 6,254,862, filed 3/02/98) for the reasons of record set forth in the Office action of 8/24/01.

Claims 13 and 20-22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Henderson et al. (U.S. 6,197,293) as applied to claims 1, 2, 4 and 10-13 above in view of Freytag et al. (Hum. Gene Ther., 9:1323-1333, 6/10/98) for the reasons of record set forth in the Office action of 3/15/01.

Claims 13 and 20-22 remain are rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al. (U.S. 6,254,862) as applied to claims 1, 2, 4 and 10-13 above in view of Freytag et al. (Hum. Gene Ther., 9:1323-1333, 6/10/98).

Applicant's arguments filed 1/10/02 have been fully considered but they are not persuasive. At page 5 of the response of 1/10/02, Applicant acknowledges that the adenoviral

vector of Henderson and Little is readable on the elected invention. Applicant argues that the Wold Declaration is sufficient to antedate the references, which have an effective date of 3/3/97.

The declaration filed on 1/10/02 under 37 CFR 1.131 has been considered but is ineffective to overcome the Henderson or Little references.

The Wold declaration is deficient in that the present application has four inventors, one of whom is Wold. The declaration is made by Wold alone and written in the first person, i.e. it appears that Wold alone invented the claimed subject matter. The declaration does not indicate whether named inventors Toth, Doronin and Tollefson are co-inventors of the elected invention. The Wold declaration indicates that inventor Doronin purified a DNA encoding the Ad5 ADP, but does not clearly indicate whether Doronin is an inventor of the elected invention. See MPEP 715.04.

The elected invention is directed to a replication-competent adenoviral vector which lacks expression of at least one of the E3 gp19K, RID or 14.7K proteins, and overexpresses the adenoviral death protein. The declaration indicates that while the instant vectors may replicate in any neoplastic cell, the Calydon vectors are restricted to liver or prostate cells. However, the claims embrace the Calydon vectors, and that is sufficient to anticipate or render obvious the rejected claims.

The evidence submitted is insufficient to establish a conception of the invention prior to the effective date of the Henderson or Little references. While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a

complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897).

The declaration refers to Exhibits A through E to support the statements made in the declaration. However, none of these exhibits were provided to the Office. Exhibit A is alleged to be a copy of the specification of application 08/277,737. The statements pertaining to this exhibit in paragraph (1) have been evaluated using the '737 application itself. Paragraph (1) points to pages 23-24 of the '737 application as evidence of conception. However, the adenovirus described in the '737 application is replication defective, and the application makes no mention of replication competent adenovirus and clearly teaches that replication defective adenovirus was the goal. Consequently, the previously described adenovirus is not embraced by the instant claims, and the '737 application cannot be used to establish conception of the instantly claimed invention at that time. The statements in paragraph (2) concerning Exhibit B cannot be evaluated since the exhibit was not provided. It is not clear from the declaration when the broad invention being claimed was conceived.

Pages 4-8 describe the construction and testing of KD1, KD3, GZ1, GZ3, and KD1-SPB adenoviral vectors. However, no evidence has been provided to substantiate these statements, e.g. copies of notebook pages, etc. It does not appear that alleged Exhibit C is evidence of construction of KD1, and alleged Exhibits D and E appear to be directed to only to testing of KD1 and KD3. These species of vectors (KD1 and KD3) are replication restricted due

specifically to the E1A mutations, and do not support the genus invention as broadly claimed, which is not limited to replication restricted vectors, or to adenovirus replication-restricted due to the E1A mutations, as opposed to placing adenoviral early genes under control of tumor-specific promoters for example. From the statements on page 6, it appears that the GZ1 and GZ3 vectors, which have wild-type E1 regions, were conceived well after the prior art was filed (over a year later). The cited prior art discloses two other species which are different in design from KD1 and KD3, and are not obvious variants of KD1 and KD3. While KD1-SPB may have been conceived on or before 10/25/96, it appears from the declaration that declarant did not enable making it until much later, at a time after the prior art was filed. See MPEP 715.03 regarding whether possession of a species, e.g. KD1 and KD2, supports a broad genus claim in an unpredictable art.

Some of the statements made are alleged to be supported by Exhibits A-E, which were not received by the Office. However, many statements do not refer to any evidentiary support. See MPEP 715.07 regarding the requirement to support statements with evidence, and the types of evidence which can be used to support the statements.

Diligence has not been addressed, since conception of the invention has not been clearly established prior to the effective date of the prior art. See MPEP 715.07(a).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 4, and 10-13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of copending Application No. 09/956,335. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims embrace the embodiment represented in the claims of the '335 application, wherein the adenovirus vector is replication restricted to cells expressing a telomerase.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Allowable Subject Matter

Claims 5, 14, 15, and 24 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX numbers are (703) 308-4242 or (703) 305-3014 for any type of communication. In addition, FAX numbers for a computer server system using RightFAX are also available for communications before final rejection, (703) 872-9306, and for communications after final rejection, (703) 872-9307, which will generate a return receipt. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

Any inquiry concerning administrative, procedural or formal matters relating to this application should be directed to Patent Analyst Patsy Zimmerman whose telephone number is (703) 308-8338. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

Scott D. Priebe, Ph.D.
Primary Examiner
Technology Center 1600
Art Unit 1632

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: Sequence Listing is incomplete, see Fig. 21.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

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